REMOVAL OF NAPROXEN AND DICLOFENAC BY HETEROGENEOUS PHOTOCATALYSIS

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Abstract
Pharmaceuticals belong to the substances which are used for treating or preventing diseases. Their global consumption is substantial. For 2015, the estimated revenue from the sale of pharmaceuticals is more than $ 700 billion. Consequence of pharmaceutical consumption is their subsequent detection in waterways, either in unchanged form or in the form of their metabolites. Pharmaceuticals from the group of NSAIDs (naproxen and diclofenac), which are often detectable at the output of waste water treatment plant were removed by heterogeneous photocatalysis. Furthermore, the influence of pH on the removal efficiency or effect of the hydrogen peroxide H_2O_2 addition was estimated. The samples were measured by high performance liquid chromatography (HPLC). Chemical and biochemical oxygen demand (COD, BOD_5) was determined as well as the inhibition of algae *Parachlorella kessleri* growth.

Key words:
Pharmaceuticals, diclofenac, naproxen, heterogeneous photocatalysis

Introduction

Pharmaceuticals are a wide group of micropollutants, which recently increased attention was given. In the European Union about 9,000 substances with therapeutic effect are registered. Likewise, the annual production of some pharmaceuticals is in hundreds of tons. Revenues from the sale of pharmaceuticals for 2015 are estimated at more than $ 700 billion. Increased consumption of pharmaceuticals leads to more frequent detection in aquatic and terrestrial environment. The reason is that the conventional waste water treatment plants are not primarily designed to eliminate this type of contaminant. Pharmaceuticals belong to the most biologically active substances, and are often synthesized to reach the biological effect at low doses (Barcelo, 2008a; Jjemba, 2008; Statista, 2015).

Diclofenac belongs to the NSAIDs (cyclooxygenase inhibitor), which causes chronic adverse effects on aquatic organisms. In the group of nonsteroidal anti-inflammatory drugs has the highest acute and chronic toxicity. Cytological changes in fish (*O. mykkis*) liver and kidney after exposure to 1 mg/l of diclofenac were reported. At higher concentrations diclofenac bioaccumulate in fatty tissues (Santos, 2010).

Naproxen belongs also among the NSAIDs. At the output of the wastewater treatment plant there were detected concentrations of tens of ng to μg/l. For both of these pharmaceuticals it was found that their degradation products are more toxic than the parent compound (Aga, 2008).

Heterogeneous photocatalysis belongs to the *Advanced oxidation processes* (AOPs), which are based on the generation of active hydroxyl radical (HO•). These methods are used to remove a broad range of pollutants in water, soil, and in the air. The redox potential of this radical is 2.8 V (compared to the redox potential of oxygen 1.23 V). Heterogeneous photocatalysis is a system composed of three parts: a catalyst, UV radiation and oxidation agents (O_2, H_2O_2). If dispersed particles are irradiated by incident radiation of a suitable wavelength, its absorption occurs on the catalyst surface. Subsequently, the positive and negative charges on the catalyst surface are formed. It leads to formation of electron-hole pairs and to the formation of reactive radicals.

The most used catalysts are oxides and sulfides of transition metals, typically titanium dioxide TiO_2. Its widespread use is due to a number of unique properties, including chemical and thermal stability. Also it is the most active catalyst between 300-390 nm (Petrovic, Barcelo 2007; Barcelo, Petrovic 2008).

The aim of this study was to verify the suitability of heterogeneous photocatalysis as a method for remove diclofenac and naproxen from model water samples. The amount of pharmaceuticals was determined by high performance liquid chromatography (HPLC). Further, measurements of chemical and biochemical oxygen demand (COD, BOD_5) were evaluated. Also ecotoxicological bioassay was conducted with algae *Parachlorella kessleri* Total chlorophyll content was determined after exposure to water samples containing diclofenac or naproxen before and after the heterogeneous photocatalysis.

Methodics

A batch reactor with a volume of 1 liter was used. Solutions of pharmaceutical and dispersed catalyst (AV-O1, Precheza Prerov, Inc.) were subsequently transferred to the reactor. The amount of TiO_2 was fixed (0.5 g/l). The initial drug concentration was 20 mg/l. This relatively high concentration was chosen because of better identification of by-products of individual pharmaceuticals during the process. As a source of UV light was applied UV-LED lamp Hellig, for which highest intensity of radiation is at a wavelength of 365 nm ± 8.5. Cooling of the whole system ensured circulation thermostat. Samples were taken at 10-minute intervals. Total time of the experiment was one hour. Each measurement was repeated twice.

Determination of the diclofenac (naproxen) content was carried out by HPLC. The volume of analyzed sample was 20 μl and separation conditions were as follows: MP = 60% ACN and 40% H_2O acidified with H_3PO_4 (to 1 liter MP 0.75 ml H_3PO_4), p = 11.2 MPa, flow rate 1 ml/min. Under these conditions the retention time was 8.3 minutes for diclofenac and 5.2 minutes for naproxen. Diode array detector (DAD) was used as a detection system. Diclofenac samples were measured at 273 nm, naproxen at 237 nm.

Ecotoxicological biotest with *Parachlorella kessleri* algae was carried out in 150 ml Erlenmayer flasks. To a 20 ml suspension of algae it was added 20 ml of pharmaceutical solution having a concentration of 20 mg/l or 20 ml of the pharmaceutical solution after photocatalytic process. Subsequently it was added 20 ml of a nutrient solution. After three days of exposure, the algae suspension was filtered on 0.2 micron syringe filter. Subsequently, chlorophyll was extracted with 4 ml of MeOH, determined by its absorbance at wavelengths of 632, 652, 666, 696 nm, as a total chlorophyll.

Results and discussion

The degradation of diclofenac by heterogeneous photocatalysis is shown in Figure 1. This graph also shows the effect of UV radiation alone and TiO_2 catalyst without UV irradiation. Experiments showed a low efficiency of diclofenac degradation when the UV is used (12%), or TiO_2 alone (10%). In contrast, heterogeneous photocatalysis (the combined effect of UV irradiation and catalyst) showed much higher efficiency. After an hour of irradiation it was achieved 91% conversion of diclofenac.

Similar results were also achieved during the naproxen photocatalysis, which are shown in the Figure 2. The removal rate by UV irradiation was 20 % and 15 % by TiO_2. Using heterogeneous photocatalysis after one hour of irradiation it was removed 96 % of naproxen.

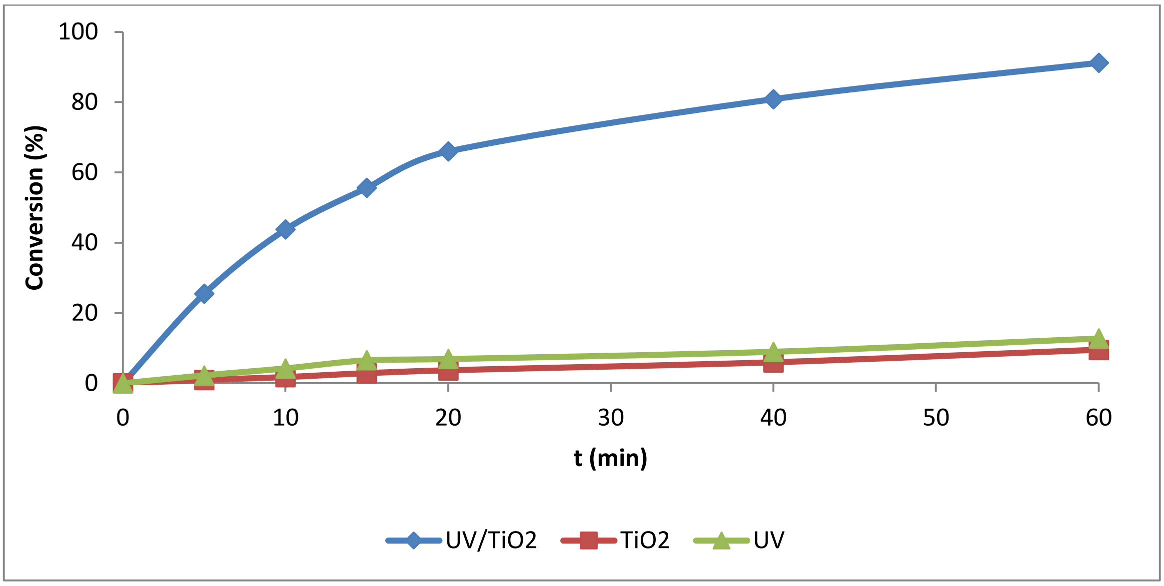

Fig. 1: Conversion of diclofenac

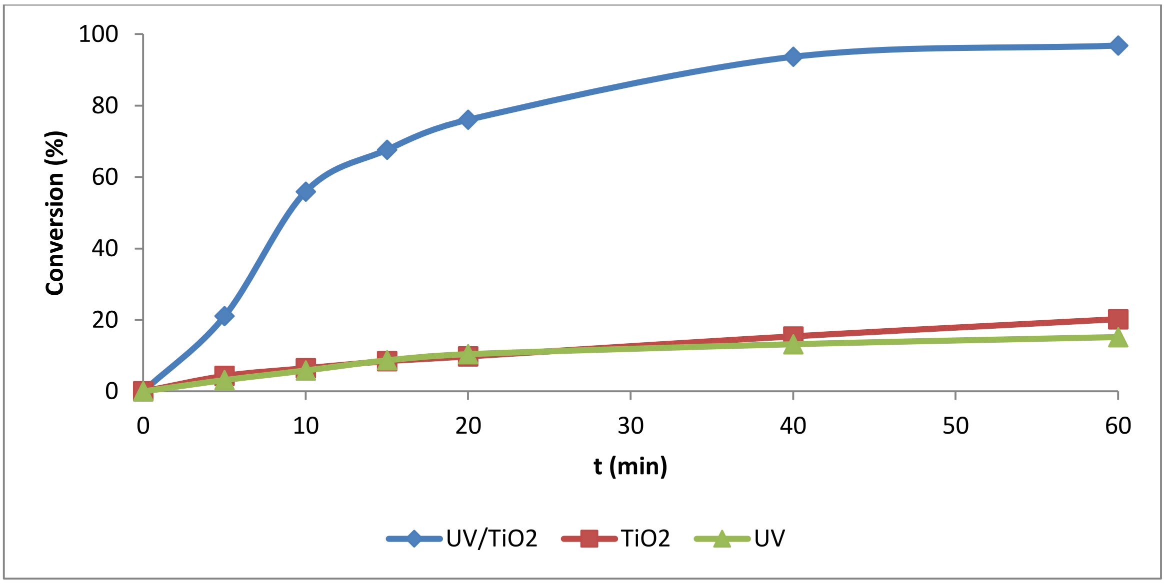

Fig. 2: Conversion of naproxen

Furthermore, the influence of the addition of 30% H_2O_2 on the removal efficiency of the individual pharmaceutical was investigated. The H_2O_2 was quantitatively transferred to the reaction vessel. The content of the peroxide was 2,5; 0,5; 0,25 g/l. The best results were achieved with a concentration of 2,5 g/l H_2O_2. The graph in Figure 3 shows that in the first 20 minutes the conversion was about 15 % faster than in the case of heterogeneous photocatalysis without addition of H_2O_2. After this time, the rate and degree of conversion practically did not differ from heterogeneous photocatalysis without addition of H_2O_2. Using lower concentrations of H_2O_2 was achieved low efficiency of removal of the drug than in the case of heterogeneous photocatalysis without addition of H_2O_2.

Conversion of naproxen by heterogeneous photocatalysis together with the addition of hydrogen peroxide is shown in the graph in Figure 4. It was observed a higher conversion rate of the drug when dose of peroxide was 2,5 g/l and 0,5 g/l. In general, however, it can be concluded that the observed addition of H_2O_2 did not affect both reaction rate and overall conversion of naproxen. Achieved conversions were practically identical to the heterogeneous photocatalysis without the addition of H_2O_2.

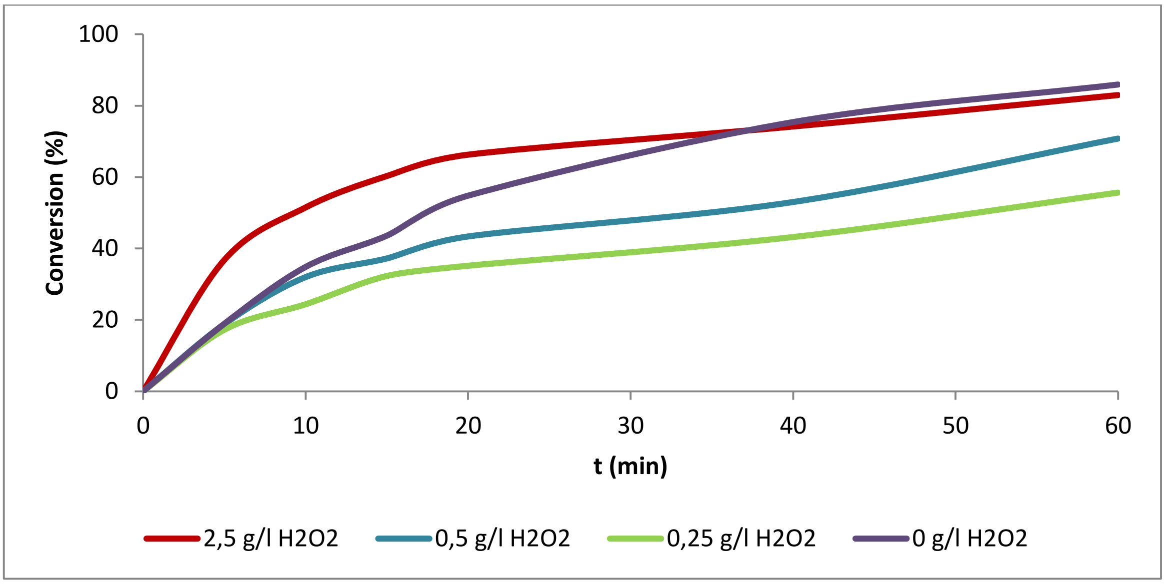

Fig. 3: Conversion of diclofenac by heterogeneous photocatalysis with H_2O_2

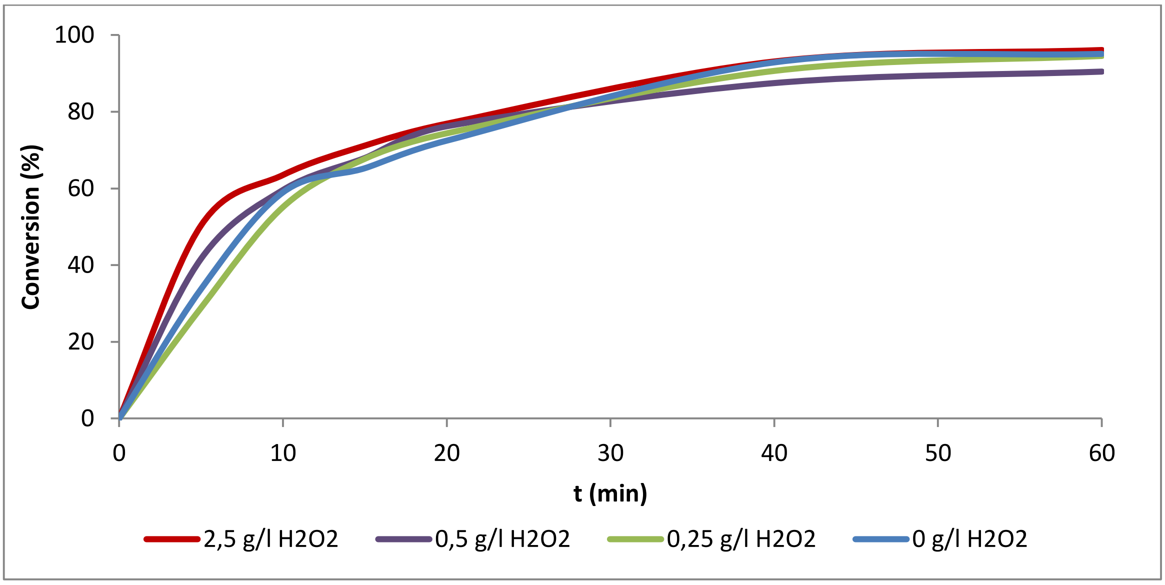

Fig. 4: Conversion of naproxen by heterogeneous photocatalysis with H_2O_2

Furthermore, the influence of pH was investigated. Diclofenac, and naproxen are very soluble acidic pharmaceutical (solubility is 50 g/l and 51 g/l), which become almost insoluble below pH 4. This phenomenon is shown in the graph in Figure 5 on the example of diclofenac. Samples were taken after one unit change of pH. Below pH 4 it was measured from the original 20 mg/l of diclofenac less than 1 mg/l of the pharmaceutical. Because in acidic medium this pharmaceuticals precipitate out of solution, photocatalysis was not applied in the acidic range and only the influence of basic pH has been investigated. It was found that adjusting the pH to an alkaline region does not affect the efficiency of removal of both pharmaceuticals from water by photocatalytic degradation. The removal efficiency was 78% for diclofenac and 93% for naproxen. Conversion of drugs in a neutral pH is not significantly different from the conversion in alkaline area.

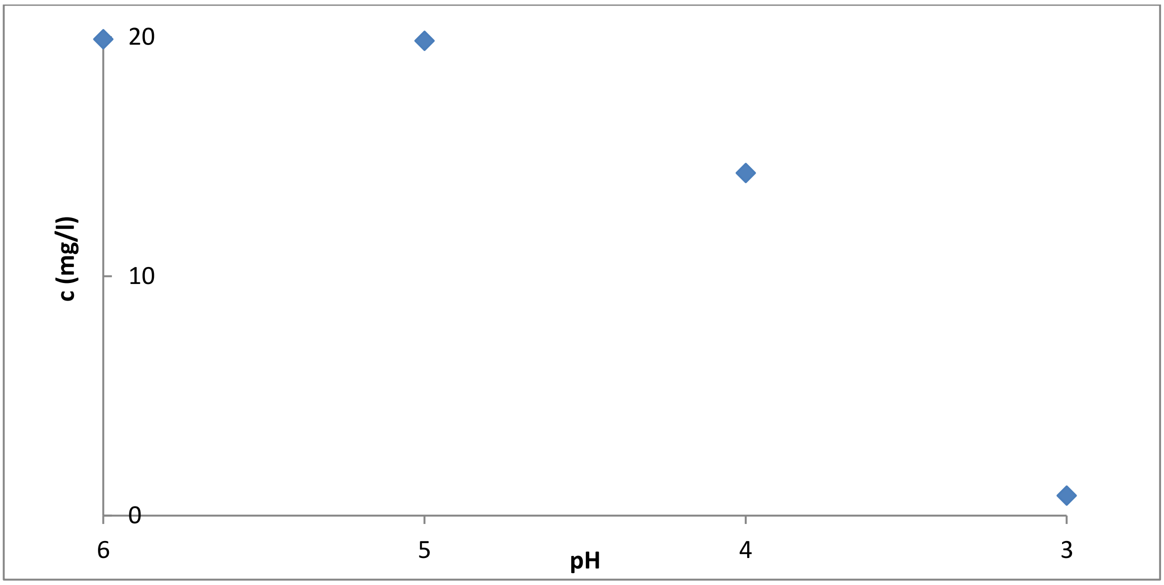

Fig. 5 Precipitation of diclofenac

Pharmaceuticals in the environment can transform into by-products that are more problematic due to their higher toxicity, or lower biodegradability. Likewise, using heterogeneous photocatalysis various intermediates may be formed from the initial organic compounds. Therefore, COD and BOD_5 were evaluated. The ratio of these two parameters determines the rate of biodegradability of the system. In the case of diclofenac and naproxen it was removed about 37 % and 23 % of the COD. BOD_5/COD ratio for diclofenac increased from 0,08 to 0,21. For naproxen the ratio increased from 0,13 to 0,17. Thus increasing ratio indicates better biodegradability of each pharmaceutical by heterogeneous photocatalysis.

Using the bioatest with *Parachlorella kessleri* it was found that although the photocatalytic process didn't lead to complete mineralization and there are detectable by-products using HPLC, total mixture after photocatalysis is less toxic to *Parachlorella* algae. Suspension of the alga was 3 days exposed to aqueous solutions of pharmaceuticals before and after heterogeneous photocatalysis. After three days, the total chlorophyll was determined and compared to controls which were not exposed. Algal growth inhibition was about 52% for diclofenac and 25% for naproxen. This inhibition was, however, reduced in algal samples exposed to a drug solution after heterogeneous photocatalysis. Subsequent growth inhibition was 36% for diclofenac and 8% for naproxen.

Conclusion

The aim of this work was to verify the suitability of heterogeneous photocatalysis for the removal of diclofenac and naproxen from model water samples. Experiments have shown that the combination of 0.5 g/l TiO_2 and radiation at a wavelength of 365 nm is able to remove over 90% of diclofenac and naproxen. Although there was no complete mineralization observed, biodegradability of the pharmaceuticals increased and toxicity to *Parachlorella* algae, which represents the producers in aquatic ecosystems, reduced. The BOD_5/COD ratio is the standard parameter to determine the biological degradation of materials. On the other hand, the ratio is non-specific parameter determining the biodegradability. It can be used more specific experiments to determine the biodegradation of pharmaceuticals- for example determining removal and biodegradability of organic compounds in the aquatic environment (simulation test with activated sludge).

Acknowledgement

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